81* A double-blind, multinational, randomized, placebo-controlled trial evaluating aztreonam for inhalation solution (AZLI) in patients with cystic fibrosis (CF), mild lung disease and *P. aeruginosa* (*PA*)

C. Wainwright[1], C. Nakamura[2], D. Geller[3], A.B. Montgomery[4]. [1]*Royal Children's Hospital, Herston, QLD, Australia;* [2]*Childrens Lung Specialists, Las Vegas, NV, United States;* [3]*Nemours Children's Clinic, Orlando, FL, United States;* [4]*Gilead Sciences, Seattle, WA, United States*

Patients (⩾6 years, FEV_1 7gt;75% predicted, *PA* positive within 3 months prior to or at screening) received AZLI (n = 76) or placebo (n = 81) TID for 28 days, with 14 days of followup. Baseline FEV_1 was 95.1% predicted. Statistically significant AZLI-placebo treatment differences were not observed at Day 28 for the primary efficacy endpoint, CFQ-R Respiratory Symptoms scores (RSS), but were observed for the secondary endpoints of *PA* density and FEV_1 % predicted (Table). At Day 28, the percentage of *PA*-positive patients decreased 20% in the AZLI group while remaining similar to baseline in the placebo group. The most commonly-reported adverse event was cough (AZLI vs. placebo: 35 [46%] vs. 31 [38%]).
Patients with baseline FEV_1 <90% predicted had larger AZLI-placebo treatment differences for CFQ-R RSS and FEV_1 % predicted than did patients with baseline FEV_1 % predicted ⩾90% (Table).

Mean AZLI–placebo treatment differences at day 28

	Overall (N = 157)	FEV1 at baseline <90% Predicted (N = 62)	FEV1 at baseline ⩾90% Predicted (N = 95)
CFQ-R RSS (points)	1.8; p = 0.44	6.7; p = 0.07	–1.4; p = 0.66
PA density (log_{10} CFUs in sputum)	–1.2; p = 0.02	–0.7; p = 0.31	–1.6; p = 0.04
FEV1 % Predicted (relative % change)	2.7%; p = 0.02	4.8%; p = 0.03	1.4%; p = 0.30

Treatment of patients with mild CF lung disease with 75 mg AZLI TID for 28 days was well-tolerated. AZLI-treated patients preserved lung function and suppressed *PA* compared with placebo. Overall effects on respiratory symptoms were modest, perhaps due to high baseline FEV_1 % predicted (95.1%) and CFQ-R RSS (72.0).

82* Safety and efficacy of tobramycin inhalation powder (TIP) in treating CF patients infected with *Pseudomonas aeruginosa* (*Pa*)

M. Konstan[1], P.A. Flume[2], F. Brockhaus[3], G. Angyalosi[3], E. He[4], D. Geller[5]. [1]*Rainbow Babies and Children's Hospital, Cleveland, OH, United States;* [2]*Medical University of South Carolina, Charleston, SC, United States;* [3]*Novartis, Basel, Switzerland;* [4]*Novartis, East Hanover, NJ, United States;* [5]*Nemours Children's Clinic, Orlando, FL, United States*

Objective: To evaluate the safety and efficacy of TIP compared to TOBI in CF patients with *Pa* infection.
Methods: Open-label, multicenter, active comparator study, comprising 3 treatment cycles (28 days on-drug followed by 28 days off-drug) in *Pa*-infected CF patients age ⩾6 yrs old randomised 3:2 to TIP (112 mg tobramycin/4 capsules) or TOBI (300 mg tobramycin/5 mL) twice daily. Safety and efficacy outcomes were evaluated.
Results: 517 patients (TIP=308, TOBI=209; 55.3% male; mean age 25.6 y, mean baseline FEV_1 % predicted 53.0) were randomised; 88% of patients experienced AEs, which were mostly mild or moderate in severity. Treatment-related AEs more commonly found in the TIP group were cough (25.3% vs 4.3%), dysgeusia (3.9% vs 0.5%) and dysphonia (12.7% vs 3.3%). A slightly greater increase in FEV_1 % predicted from baseline to end of Cycle 3 was observed with TIP (5.8) compared to TOBI (4.7) [LS mean difference: 1.1; lower bound of 1-sided 85% CI=-0.67]. Mean change in sputum density of *Pa* biotypes (log_{10}CFU/g) was comparable within treatments across the 3 cycles and greater with TIP compared to TOBI. The distribution of tobramycin MIC of *Pa* isolates was relatively consistent over the course of study. Anti-Pseudomonal antibiotics other than inhaled tobramycin were more commonly used in the TIP group, but for a shorter average time than in the TOBI group.
Conclusion: Overall TIP safety profile was similar to TOBI, except certain local tolerability side effects which may be related to the relatively high amount of powder with TIP. TIP had numerically slightly better efficacy (FEV_1 and *Pa* density) than TOBI.

83 Treatment convenience and satisfaction of tobramycin inhalation powder (TIP) versus TOBI in cystic fibrosis (CF) patients

D.E. Geller[1], P.A. Flume[2], F. Brockhaus[3], J. Zhang[4], G. Angyalosi[3], E. He[4], M. Konstan[5]. [1]*Nemours Children's Clinic, Orlando, FL, United States;* [2]*Medical University of South Carolina, Charleston, SC, United States;* [3]*Novartis, Basel, Switzerland;* [4]*Novartis, East Hanover, NJ, United States;* [5]*Rainbow Babies and Children's Hospital, Cleveland, OH, United States*

Objective: Nebulised therapy places a time burden on CF patients. We evaluated the convenience and satisfaction with a new formulation of tobramycin (TIP) compared with TOBI.
Methods: Open-label, multicenter, active comparator study in CF patients age ⩾6 years with *Pseudomonas aeruginosa* (*Pa*) infection. Patients were randomised (3:2) to TIP (112 mg tobramycin/4 capsules) administered via dry powder inhaler or TOBI (300 mg tobramycin/5 mL) administered via PARI LC Plus nebuliser twice daily for 3 treatment cycles (28 days on-therapy followed by 28 days off-therapy). Self-reported satisfaction was measured using the modified Treatment Satisfaction Questionnaire for Medication (TSQM) factored into four domains: Effectiveness, Side Effects, Convenience, and Global Satisfaction.
Results: 517 patients (TIP = 308, TOBI = 209; 55.3% male; mean age: 25.6 y, mean baseline FEV_1 %predicted 53.0) were randomised. Treatment satisfaction was significantly higher for TIP than TOBI at all visits for the effectiveness ($P < 0.0001$), convenience ($P < 0.0001$), and global satisfaction ($P = 0.0018$). There was no difference in side effects ratings between groups nor were there any changes in satisfaction scores within treatment groups over time. The overall administration time for TIP (median: 5.6 min) was 14 min less than TOBI (19.7 min) supporting the results of TSQM regarding convenience and global satisfaction.
Conclusion: CF patients rated TIP as more convenient and satisfying than TOBI for treating *Pa* infections, consistent with the shorter treatment time for TIP.

84 *In-vivo* data support equivalent therapeutic efficacy of a new tobramycin inhalation solution (150 mg/1.5 ml) administered by the eFlow® electronic nebuliser compared to TOBI® in the PARI LC PLUS®

M. Keller[1], A.L. Coates[2], M. Griese[3], O. Denk[1], J. Schierholz[1], M. Knoch[1]. [1]*PARI Pharma GmbH, Aerosol Research Insitute, Graefelfing, Germany;* [2]*Hospital for Sick Children, Toronto, ON, Canada;* [3]*Haunersches Children Hospital, Munich, Germany*

Aims: Two clinical studies were conducted to demonstrate equivalent lung deposition and safety in CF patients for a new tobramycin inhalation solution 150 mg/1.5 ml (Tobramycin PARI) delivered by an investigational eFlow® electronic nebuliser in comparison to TOBI® (300 mg/5 ml) administered by the PARI LC PLUS® breath enhanced jet nebulizer powered by a PARI BOY® N compressor.
Methods: Lung deposition of two ^{99m}TC-DTPA labelled tobramycin solutions was investigated in a cross over study design. The inhalation of TOBI® via the PARI LC PLUS® and Tobramycin PARI via an investigational eFlow nebulizer was studied in 16 CF patients (8 children and adults, each). Above medications were inhaled twice daily in a second safety study, conducted in 76 CF patients (38 adults and children, each) in a parallel design for 28 days. After 7 days, Tobramycin was assessed from sputum, and Cmax, AUC from blood plasma.
Results: See the table; all results are mean values.

Comparison of TOBI and Tobramycin PARI

Group	Lung deposition [mg]		Sputum concentration [mg/L]		Cmax [mg/L]	
	TOBI	Tobramycin PARI	TOBI	Tobramycin PARI	TOBI	Tobramycin PARI
All patients	45.4	46.0	2.27	2.59	1.65	1.29
Adults	46.8	45.6	2.65	2.67	1.81	1.21
Children	44.1	46.4	1.99	2.50	1.52	1.36

Conclusions: No statistically significant differences were found regarding lung deposition and sputum concentration being efficacy parameters, but significant differences regarding AUC ($p < 0.005$ to $p < 0.001$) and Cmax ($p = 0.02$ and $p < 0.001$) being a safety parameter. Inhalation time for Tobramycin PARI by an investigational eFlow® was significantly ($p < 0.0001$) shorter (4.6 vs. 16.1 min) vs. TOBI®/LC PLUS® and may help to improve patients' quality of life and drug adherence.